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Investigating the Relationship Between Infant Bronchiolitis Severity and Early Childhood Asthma

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To the Editor:

In response to our recent article¹ Piippo-Savolainen et al. share data from their well- studied cohort of 83 subjects followed from early childhood for over 25 years for asthma and other pulmonary outcomes.² Several factors make it difficult to make comparisons to our recent findings from the work highlighted by Piippo-Savolainen et al. including: the small sample size, the fact that their study was neither designed nor powered to address our study questions, differences between studies in how exposure and outcome variables were defined,

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and the lack of both a spectrum of bronchiolitis severity and a comparison group without bronchiolitis.

Our population-based retrospective birth cohort study, the Tennessee Asthma Bronchiolitis Study (TABS), was designed to investigate the relationship between infant bronchiolitis and early childhood asthma. The definition of the risk factor of interest, bronchiolitis during infancy, differs significantly between the studies. Our measure of bronchiolitis severity was based on level of health care for bronchiolitis, including clinic visits, emergency department visits, and hospitalizations, as determined by ICD-9 diagnosis, with the risk period being only during infancy. Our inclusion of a comparison group of infants, who had no visit for bronchiolitis in their first year, allowed for the hypothesis-driven investigation of whether there was a severity-response relationship between the most advanced level of health care for bronchiolitis and subsequent early childhood asthma risk and morbidity. Piippo-Savolainen et al. have followed 83 children who were all hospitalized for bronchiolitis at <24 months. Piippo-Savolainen et al. also compare results from sub-analyses aimed at investigating the relationship of what they term “invasiveness” of the child index illness as determined by infiltrate on chest radiograph, and subsequent asthma outcomes to previously published work by Castro-Rodriguez et al.³ Our study was not designed to investigate this question.

In regard to the authors’ concluding comments regarding asthma following non-RSV bronchiolitis, we have previously shown that bronchiolitis occurring during rhinovirus (RV)-predominant months was associated with an estimated 25% increased risk of early childhood asthma compared with bronchiolitis occurring during respiratory syncytial virus (RSV)-predominant months.⁴ This work supports recent findings that early RV-wheezing illnesses are associated with higher risk of subsequent asthma than other viruses.⁵ However, as we’ve seen in our Tennessee Children’s Respiratory Initiative prospective investigation, the burden of RSV bronchiolitis during infancy is much greater than RV bronchiolitis. Therefore the expected number of asthma cases following infant RSV bronchiolitis would likely be much greater.

Importantly, the work by Piippo-Savolainen et al. does highlight what has been demonstrated in other longitudinal investigations, that the proportion of children who persist in having a post-infant bronchiolitis asthma phenotype may vary with age through childhood.^{6–8} The report of the high prevalence of subnormal lung function following infant infection in their cohort is also interesting. This suggests that early severe viral respiratory infections may either lead to lung function abnormalities, or infants with abnormal lung function are predisposed to develop these infections. Clinical trials aimed at preventing severe viral infections during infancy will ultimately elucidate the nature of the association between infant viral respiratory tract illnesses and the development of early childhood asthma.

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